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THE STREPTOCOCCO-OPSONIC INDEX IN SCARLATINA.*

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ON account of the close association of streptococci with scarlatina, it was thought that it would be of interest to study the streptococco-opsonic power of the blood throughout the course of this disease.

TECHNIQUE.

The Leishman-Wright method of estimating the opsonic index has been employed in these examinations: Equal volumes of serum, washed corpuscles, and streptococcal suspension are thoroughly mixed in a capillary pipette and the mixtures incubated at 37° C. for 15 minutes, when smears are made and stained. The streptococcal suspension is made from a 24-hour culture on plain agar, or horse-serum agar if the organism does not grow well on the plain agar. The fluid of condensation is discarded because of the clumps and long chains of cocci that it usually contains. The growth on the solid medium is washed off with enough 0.85 per cent salt solution to produce a slightly opalescent fluid. An effort is made to obtain a suspension of sufficient thickness to give an average count of five organisms per leucocyte in the normal specimen.

The sera from three normal individuals is pooled and used as the normal control. The pool is collected the same day as the patient's serum, but both may be kept 24 hours before the index is determined. Blood from the same individuals is generally employed for the pool, and the washed blood (leucocytes) obtained from an individual whose erythrocytes are not susceptible to isoagglutination. Fifty polymorphonuclear neutrophiles are counted, 25 at each end of the slide. If these two counts do not correspond closely, more leucocytes are counted. If the suspension is thin, so that there is an average of 1–3 organisms per leucocyte, 100 cells are counted. When the suspension is thin, the percentage of phagocyting cells is estimated. Generally this percentage index corresponds closely to the opsonic index. Clumps of leucocytes are disregarded.

OBSERVATIONS ON STREPTOCOCCO-OPSONIN

It is now well known that normal human serum as well as the serum of many animals contains opsonin for various strains of streptococci.

In a large number of preliminary tests I found that the streptococco-opsonic index of normal adult persons may vary between 0.90 and 1.1. In these experiments as well as in the earlier experiments with the sera of scarlet fever patients a typical *Strept. pyogenes*, isolated by Dr. Ruediger from a case of otitis media in scarlatina and which ferments mannit, was employed by preference, not only on account

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of its source but also because of its relatively uniform suspensions. In order to determine to what extent the opsonic index in case of this particular strain ("Laura") could be regarded as true for other similar strains, a number of comparative tests were made. As shown in Table 1, only slight variations were detected, and most of the observations recorded here have been carried on with streptococcus "Laura" controlled, however, from time to time by the use of streptococcal strains isolated from the very patients whose sera were being studied.

TABLE 1.

COMPARATIVE STREPTOCOCCO-OPSONIC INDICES OBTAINED WITH STREPTOCOCCUS "LAURA" AND HOMOLOGOUS STREPTOCOCCI.

SERUM "A"		SERUM "B"		SERUM "C"		SERUM "D"		SERUM "E"	
Strept. "Laura"	Strept. "A"	Strept. "Laura"	Strept. "B"	Strept. "Laura"	Strept. "C"	Strept. "Laura"	Strept. "D"	Strept. "Laura"	Strept. "E"
1.34	1.7	1.7*	0.77*	1.4	1.0	1.4	1.2	1.24	1.4
1.0	1.0	1.3	1.7	1.3	1.28	0.89	0.99	1.0	0.9
0.94	0.94	0.98	1.2	0.97	1.0	1.0	1.1		
1.26	1.28	1.2	1.5	0.91	0.89				
0.9	0.9	1.2	1.1	1.09	1.1				
1.28	1.2								
1.14	1.0								
1.18	1.2								

Serum "A" from scarlet-fever patient with cervical abscess from pus of which streptococcus "A" was isolated.

Serum "B" from scarlet-fever patient with otitis media from pus of which streptococcus "B" was isolated.

Serum "C" from erysipelas patient; streptococcus "C" isolated from abscess in leg.

Serum "D" from scarlet-fever patient; streptococcus "D" isolated from throat.

Serum "E" from scarlet-fever patient; streptococcus "E" from throat.

* No evident explanation at hand for this divergence.

It was considered possible that heating the normal and scarlatinal sera might bring out greater differences in the opsonic indices. While this proved to be the case in occasional instances (Table 2),

TABLE 2.

STREPTOCOCCO-OPSONIC INDICES OF HEATED AND UNHEATED SCARLATINAL SERUM.

Unheated	Heated	
1.43	1.60	55° C. one hour
1.30	1.30	
1.30	1.20	
1.00	2.50	
1.20	1.90	
0.96	0.99	
0.96	1.00	
0.97	0.94	
0.86	0.84	
1.60	1.30	
1.40	1.30	60° C. 30 min.
1.36	1.70	

the indices in general were found to remain about the same as when unheated sera were used. Heating human serum (normal and scarlatinal) to 55° C. for one hour reduces the streptococco-opsonic power very materially; heating to 60° C. for half an hour reduces the opsonin content to a fraction of the normal.

Dilutions of serum with 0.85 per cent NaCl solution gave about the same indices as the undiluted serum when the relation of serum to solution was as 1:10 and 1:20; in higher solutions in some cases the scarlatinal sera gave very high indices, but for the present purpose it was thought best to follow the usual methods.

The specificity of streptococco-opsonin in scarlet fever.—During the course of this investigation the opsonic index of scarlet-fever patients with respect to staphylococci, pneumococci, *Strept. viridans* and pseudodiphtheria bacilli has been determined repeatedly. The results may be summarized in the statements that the opsonic index for staphylococci, pneumococci, and *Strept. viridans* was found to be normal on all occasions while that for *Strept. pyogenes* varied from 0.5–2.6; nor was there any correspondence in two cases examined between the streptococco-opsonic index and the index for the pseudodiphtheria bacilli isolated from the suppurating ears in these instances. The streptococco-opsonic index of uncomplicated cases of measles and of typical pneumonia was found to range wholly within normal limits (0.96–1.1). In erysipelas, however, the streptococco-opsonic index was found to present a sharp rise at about the time the temperature began to fall. In diphtheria there is also a rise in the streptococco-opsonic index early in the disease. These facts seem to me to indicate that the streptococco-opsonin in scarlet fever is a specific opsonin.

THE STREPTOCOCCO-OPSONIC INDEX IN SCARLET FEVER.

The blood of 16 scarlatinal patients has been examined, generally daily during the acute stage and at greater intervals during convalescence. In 10 cases during the acute stage the opsonic index was found below 0.9, ranging from 0.5 to 0.88; in five between 0.9 and 1.0; and in one only not below 1.0. As I found the normal opsonic index to streptococci to vary between 0.90 and 1.1, the cases with indices of 0.9 can scarcely be considered outside the normal limit.

With the fall in temperature and improvement in the patient's symptoms there occurs a rise in the index to above normal; this was true of all my cases except in a quickly fatal case in which the index did not rise above 1.0. In seven cases, all complicated, the opsonic index rose above normal while the fever was still high, but at this time there seemed in each case to be an improvement in the general condition.

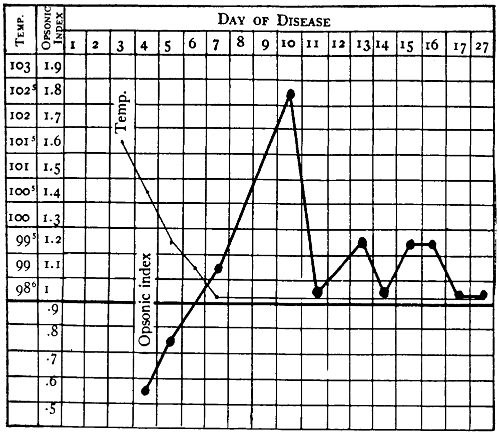

Chart 1.—Mild, uncomplicated scarlet fever. (Male, age 16.)

This usual rise in the index is succeeded by a fall to normal, often more or less abrupt, as may be seen in Charts 1, 2, 3, as well as others. The index remains at or near normal during convalescence in less severe, uncomplicated cases. Chart 4 shows the fluctuations of the index in a severe case without evident special complications.

The cases (six) in which the opsonic index at first examination was not below normal were not observed until on the 5th–7th day, and at this time the index may have recovered from the initial fall. In two of these cases diphtheria coexisted with scarlet fever, but without any special effect upon the course of what may be regarded as the typical streptococcus-index of scarlet fever.

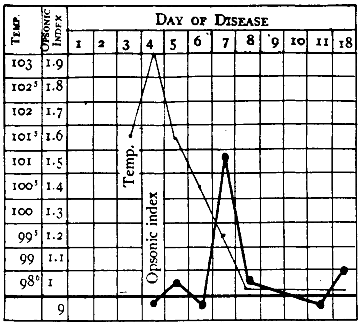

Chart 2.—Mild, uncomplicated scarlet fever. (Adult female)

In the cases that were free from special complications during the early part of the attack, the rise of the index above normal occurred between the 5th and 11th days; most often between the 7th and 9th. According to the observations of Bowie[1], Klotz,[2] Tileston and Locke,[3] this is also about the time when the leucocytosis of scarlet fever is at its height. The polymorphonuclears are now relatively increased. This coincidence of the streptococco-opsonic curve and the leucocytosis may be regarded as marking the high level of the streptococcidal powers of the blood in scarlet fever.

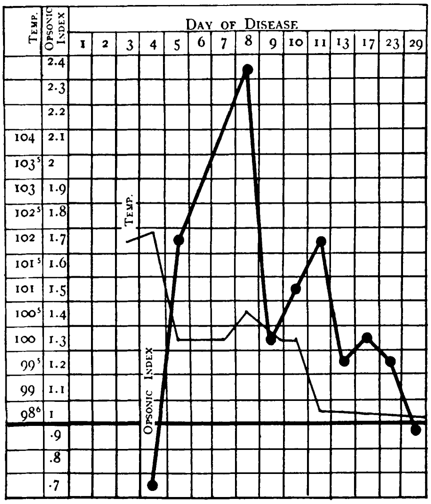

Chart 3.—Mild, uncomplicated scarlet fever. (Male, age 10.)

In the cases in which the indices showed a tendency to remain above normal for some time after the primary rise there occurred no streptococcal complications. Definite local streptococcal complications appear to be

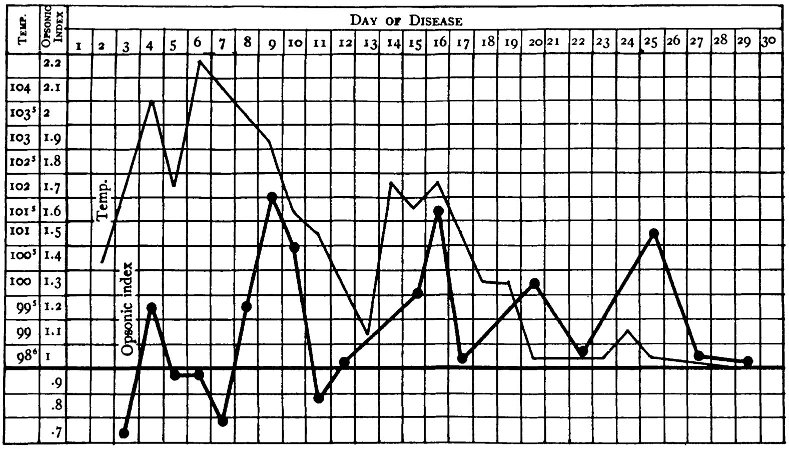

Chart 4.—Severe scarlet fever. (Female, age 12, no special complications; recovery.)

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[1] *Jour. Path. and Bact.*, 1902, 8, p. 82.

[2] *Jour. Infect. Dis.*, 1904, 1, p. 404.

[3] *Ibid.*, 1906, 3, p. 375

initiated with low streptococco-opsonic indices; as improvement takes place, the indices commonly rise (Charts 5, 6, 7). Although no cultures were made from the joints in the case illustrated on Chart 5, the course of the index indicates the streptococcal nature of the articular lesion.

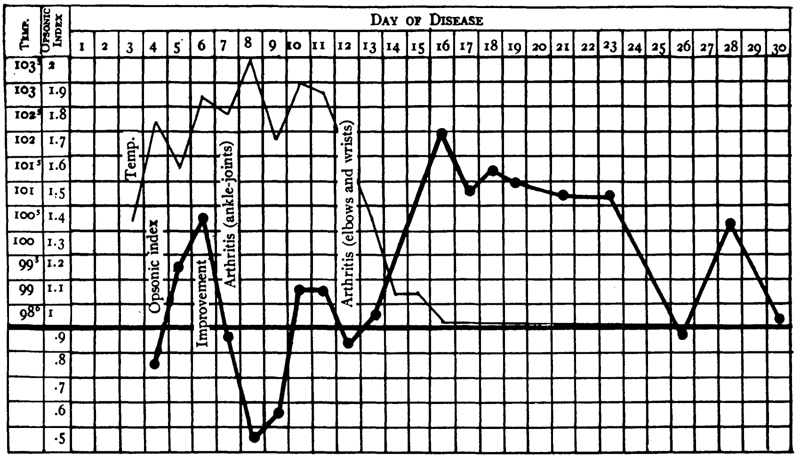

Chart 5.—Severe scarlet fever with joint complications. (Male, age 13; recovery.)

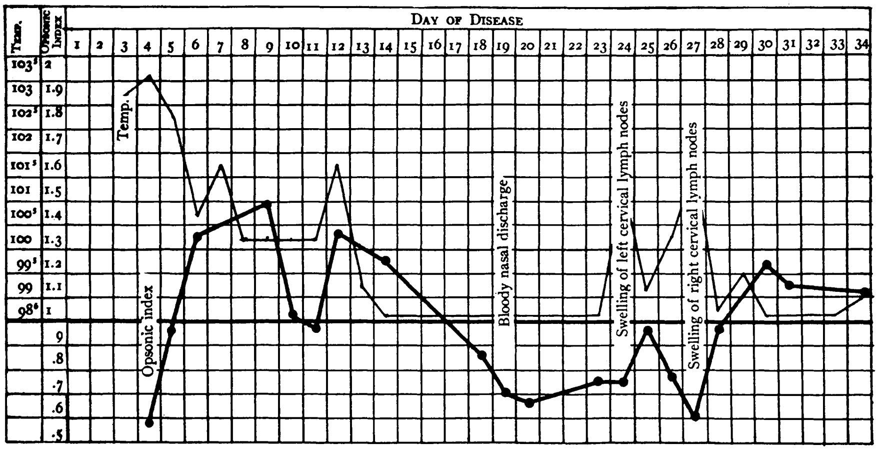

Chart 6.—Severe scarlet fever with cervical lymphatic involvement. (Male, age 14; spontaneous resolution; recovery.)

In two cases of postscarlatinal streptococcal otitis (not included in the 16 cases discussed here) the indices rose above normal as the discharge diminished. In otitis media due to other bacteria, e. g., pseudodiphtheria bacilli, the streptococcal index did not vary in any such accord with the clinical course of the infection.

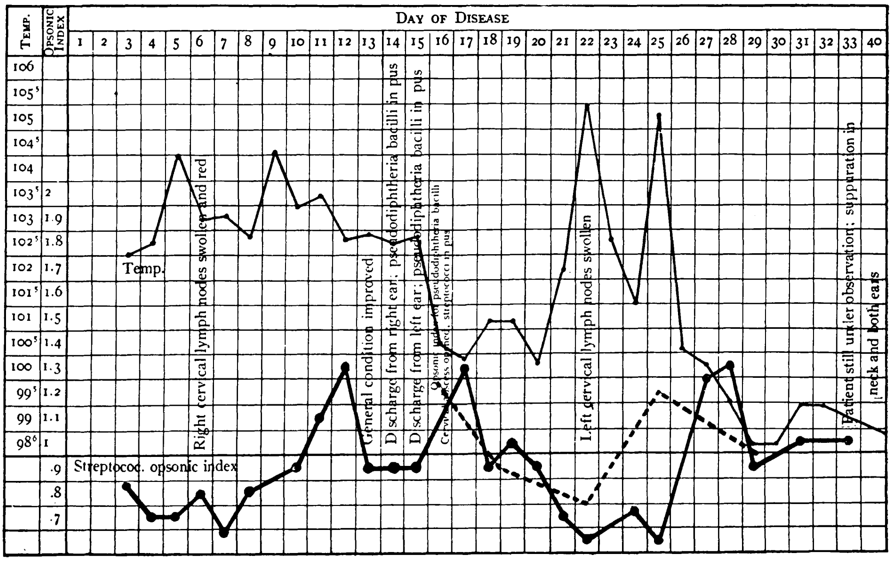

CHART 7.—Scarlet fever with suppuration in cervical lymph nodes and ears. (Female, age 5; recovery.)

In a fatal case complicated by broncho-pneumonia, the streptococco-opsonic index gave a sharp primary rise (Chart 8) with an abrupt fall coincidently with the onset of the pneumonia. During the rest of the illness the index remained about normal. A few days before death, cultures of the blood gave streptococci in pure growth. The cause of the pneumonia was not determined and there was no autopsy. Judging from Chart 8 there was after the 11th day of the prolonged illness in this case no marked reaction of the organism to streptococcal products. Whether this should be interpreted as meaning that the streptococcus played no special part in the subsequent events or was the result of failure of response on the part of the organism, must be left unsettled.

It may be of interest to mention again that in diphtheria there occurs a sharp rise in the streptococco-opsonic index somewhat earlier in the disease than seems to be the case in scarlet fever and, so far, the streptococcal index has not been found below normal in the acute

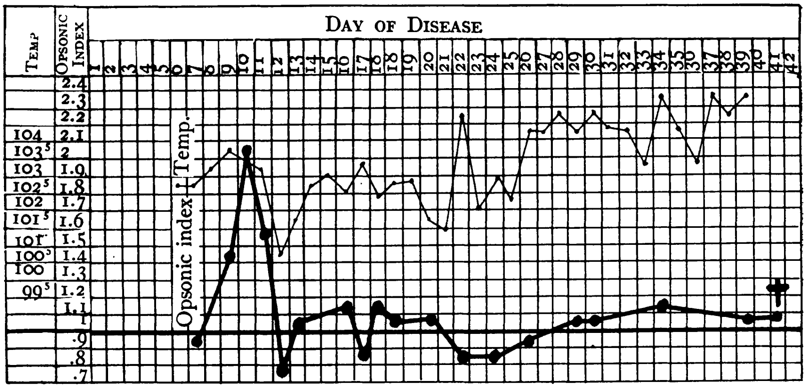

CHART 8.—Scarlet fever, broncho-pneumonia; death. (Female, age 15; broncho-pneumonia developed about 11th day; no tubercle bacilli in sputum; tuberculo-opsonin index at one time .7; terminal streptococcemia.)

stage of diphtheria. The index for diphtheria bacilli in diphtheria is low at the outset, rising above normal quite considerably as the membrane disappears and the symptoms abate.

THE RELATION OF STREPTOCOCCI TO SCARLET FEVER AND CONCLUSIONS.

The results of this study are fully in accord with the view that streptococci play an important part in scarlet fever. The variations in the streptococco-opsonic index even in mild cases, show that practically from the first the scarlet-fever patient is the subject of a definite streptococcus infection. The course of the index indicates that this infection runs parallel with the phenomena of the acute stage of the attack and hence must be held responsible for at least some of these phenomena.

There is no question concerning the streptococcal nature of most of the complications of scarlet fever and as would be expected such complications influence the streptococco-opsonic index accordingly, there being an initial fall succeeded by a definite rise as the infection subsides. The conditions in the severe, so-called "septic" cases merit further study. Investigations are also under way for the purpose of determining the preventive and therapeutic effects of streptococcus vaccine in scarlet fever and its complications.

At present the following conclusions seem warranted:

In the beginning of scarlet fever the streptococco-opsonic index in the majority of cases is below normal. As the acute symptoms subside the index rises above normal to which it soon returns, sometimes quite abruptly. In uncomplicated cases it commonly remains practically normal during convalescence. Definite local streptococcal complications are inaugurated by a depression in the streptococco-opsonic index which rises again as improvement takes place.